REMARKS

Applicants file this response concurrently with a Request for Continued Examination and respectfully request the withdrawal of the finality of the outstanding office, and consideration of the present amendment and response.

I. Status of the Application

Claims 1-24 were filed originally. Claims 1-4 and 17-24 were canceled in a previous response. Claims 11-16 are canceled herein. Claims 25-42 are new claims. Support for the new claims may be found at least on pages 8-14. Thus, claims 5-10 and 24-42 are currently pending.

II. Rejections under 35 U.S.C § 103

The Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The Examiner has failed to satisfy all three requirements for establishment of obviousness under 35 U.S.C. §103.

A. Rejection of Claims 5-9 and 11-15 as Obvious in light of Goldstein in view of McDonald.

Claims 5-9 and 11-15 are rejected under 35 U.S.C. §103 as being obvious in light of Goldstein *et al.* (U.S. Patent 5,962,427), in view of McDonald *et al.* (U.S. Patent 6,120,799). Applicants respectfully traverse.

The claimed invention is directed a method of enhancing wound healing by direct application of cholesterol-containing cationic liposomes containing DNA encoding growth factors. The claimed methodology improves wound healing while decreasing the hypermetabolic response which results in lean body tissue loss, acute phase responses such as inflammation, and compromised immune response.

In contrast, Goldstein et al. teach the facilitation of wound healing in conjunction with exposing cells migrating into the a gene activated matrix to DNA encoding growth enhancing proteins. Notably the novel aspect of the gene activated matrix of Goldstein is the presence of naked DNA encoding the growth factors. Goldstein states in column 8 that "Surprisingly, these repair cells, which are normally difficult to efficiently transfect, whether in vitro or in vivo, are extremely efficient at taking up and expressing DNA when activated to proliferate by the wound healing process." Implied in Goldstein's comments in column 5 that read

> "Specifically, it is shown that the method of the invention overcomes the problems associated with currently available gene therapy protocols. [as described in the background section in columns 3 and 4 include liposomal formulations] ... By analogy, the DNA acts much like "bait" in a "trap": the DNA is encountered by unwitting repair cells that have proliferated and then migrated into the gene activated matrix. These cells, in turn, are surprisingly capable of taking up DNA and expressing it as a therapeutic agent." (Comment inserted)

is that the DNA is not associated with liposomes and should not be associated with such. Given these "surprising" results one of skill in the art would have no expectation that substitution of liposomes for the naked DNA would be successful, hence there can be no expectation of success and no *prima facie* case of obviousness. In fact, Goldstein teaches away from using liposomes by implicitly requiring DNA to be in the form of naked DNA. There is nothing in either Goldstein or McDonald that implicates liposome associated DNA to the operative in the Goldstein invention. Thus, the only source for such an inference is the present application, which is impermissible hindsight.

Furthermore, McDonald teaches intravenous injection of cationic liposomes containing DNA encoding proteins that stimulate angiogenesis, but does not teach the direct application of cationic liposomes in conjunction with a wound coverage material. Therefore, one of skill in the art would not be motivated to combine the liposomes of McDonald et al. with the DNA and wound coverage materials of Goldstein et al. because neither reference provides any evidence that the liposomes will be effective when directly applied to a wound. In fact, Applicant respectfully submit that McDonald et al. teaches away from the instant invention in that McDonald et al. teaches that the liposomes are preferentially taken up by angiogenic endothelial cells in vascular tissues (Column 13, lines 50-54).

In contrast, to affect the hypermetabolic response to thermal injury the liposomes of the instant invention were used to efficiently transfect DNA into many different cell types including dermal cells, myofibroblasts, endothelial cells, and macrophages. Therefore, one of skill in the art would assume that, at best, liposomes would only be effective-in delivering DNA to capillary endothelial cells or migrating repair cells at the wound site if combining McDonald and

Goldstein, which fails to obviate the present invention. Thus, the claims cannot be considered under 35 U.S.C. §103(a) as being obvious over Goldstein et al. in view of McDonald et al. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

B. Rejection under 35 U.S.C § 103

Claims 5, 9, 11 and 15 are rejected under 35 U.S.C. §103 as being obvious in light of Goldstein *et al.* (U.S. Patent 5,962,427) and McDonald *et al.* (U.S. Patent 6,120,799) in view of Coleman *et al.*, (U.S. Published Application 2003/0018984). Applicants traverse this rejection.

Goldstein and McDonald have been discussed supra. Coleman et al. teaches gene delivery vectors for controlled expression of recombinant IGF-I genes within tissues at certain levels (see abstract). Even though Coleman et al. briefly mentions that IGF-I encoding expression vector is effective for use to treat an external wound as a result of a nerve crush, Coleman et al. does not use cholesterol-containing cationic liposomes to deliver the DNA construct. Coleman et al. provides no teachings that overcome the deficiencies of Goldstein and McDonald in rendering obvious the instant invention. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

C. Rejection under 35 U.S.C § 103

Claims 5-8 and 11-14 are rejected under 35 U.S.C. §103 as being obvious in light of Goldstein *et al.* (US Patent 5,962,427) and McDonald *et al.* (US Patent 6,120,799) in view of Baur (US Patent 4,361,552); Boyce (US Patent 5,976,878); and Kushner (US Patent 5,741,509). Applicants traverse this rejection. Goldstein and McDonald have been discussed supra. The additional references provide no teachings that overcome the deficiencies of Goldstein and

McDonald in rendering obvious the instant invention. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

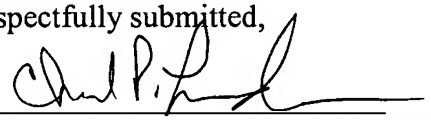
Conclusion

For the foregoing reasons, the Examiner is respectfully requested upon continued examination of the present application to withdraw the finality of the Office Action, consider the amended claims, and find that the application is in condition for allowance. The Examiner should feel free to contact the undersigned representative if any questions, comments, or suggestions arise.

Applicant believes no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. CLFR:184USD1 from which the undersigned is authorized to draw.

Dated: September 16, 2005

Respectfully submitted,

By 

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